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Original article

A comparative study of antioxidant defenses and lipid profile in premenopausal and postmenopausal osteoporotic women

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ABSTRACT

BACKGROUND: Osteoporosis is a condition of reduced bone mineral density (BMD) which leads to increased bone fragility and a marked increase in the risk of fractures. Postmenopausal osteoporosis affects women from one to twenty years after menopause. During these years, menopausal hormonal changes cause alterations in the serum levels of various biochemicals which reflect the bone losses. OBJECTIVE: The purpose of this study was to evaluate the status of some antioxidants and lipid profile along with lipid per oxidation in postmenopausal osteoporotic women. METHOD(S): Vitamin C, glutathione per oxidase (GPX), superoxide dismutase (SOD), plasma malondialdehyde (pMDA) and lipid profile were estimated in the blood of postmenopausal osteoporotic women (n=56) and compared with those in the premenopausal women treated as control (n=56). RESULTS: In the postmenopausal osteoporotic women a highly significant decrease in the GPX, SOD, vitamin C and high density lipoprotein cholesterol (HDL- c) and a highly significant increase in the pMDA, total cholesterol (TC), triglycerides (TG) and low density lipoprotein cholesterol (LDL- c) was observed as compared to the same in control group. A significant increase in very low density lipoprotein cholesterol (VLDL- c) was also observed in the postmenopausal group. CONCLUSION: Postmenopausal osteoporotics showed lower antioxidant defenses compared to premenopausal women and oxidative stress in the study group was subsequently responsible for the oxidative injury resulting in pathology. The oxidative stress markers may be important indicators for bone loss in postmenopausal women. The mechanism underlying antioxidants and its relevance to pathogenesis of osteoporosis however deserve further research.

1. Introduction

Osteoporosis is a skeletal disease characterized by low bone mass and structural deterioration of bone leading to bone fragility [1]. The increased bone fragility directly increases the susceptibility to fracture, especially of hip, spine and wrist, although any bone can be affected [2, 3].Osteoporosis related bone fractures are significant cause of mortality and morbidity, with elderly postmenopausal women being particularly affected. It moves quickly with up to 20% of expected lifetime bone loss occurring within the first 5-7 years after menopause. Menopause is a gradual three stage process that concludes with the cessation of periods and reproductive life of women. When a woman's menstruation has ceased spontaneously at least for a year, it is menopause [4]. In post menopause ovaries stop making estrogen which has got strong antioxidant properties. Deficiency of estrogen affects the antioxidant enzyme system. Estrogens tend to decrease the low density lipoprotein cholesterol (LDL) and increase the high density lipoprotein cholesterol (HDL), affecting the lipid metabolism thus. The beneficial effects of estrogens might be attributable to their free radical scavenging structure [5].

Menopause is a phase in process of aging and estrogen is supposed to play a role in modulation of aging process. Aging progresses as a result of free radical damage. Free radicals have been proposed as important causative agents of aging [6].

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Menopausal women are likely to develop oxidative stress (OS) because of the advancing age and of course due to the deficiency of estrogen. Oxidative stress is a biochemical disequilibrium propitiated by excessive production of free radicals and reactive oxygen species (ROS), which provoke oxidative damage to biomolecules and is linked with aging and several chronic degenerative diseases among which osteoporosis is found [7, 8]. Enzymatic and non enzymatic antioxidant defenses present in the plasma and erythrocytes neutralize the oxidative stress induced damage.

The purpose of this study was to evaluate antioxidant defenses of elderly osteoporotic women.

2. Materials and Methods

Study was carried out at Bafna Hospital and Research centre, Indore. The study population included 56 premenopausal women aging 25-40 years and an equal number of postmenopausal women aging between 55-65 years. Postmenopausal women with a T-Score of -2.5 or less at left femur were included in the study. Postmenopausal women on hormone replacement therapy were excluded. All ethical measures were followed prior to the study and written consent from the study group was obtained.

Bone mineral density (BMD) was measured at Sampoorna Sodani Diagnostics, Indore by Dual X-ray Absorptimetry (DXA) using the lunar DPX DXA system (analysis version: 10.51) manufactured by GE health care. Subjects underwent a fasting blood withdrawal on the day of bone scan. Blood samples were analyzed for lipid per oxidation [9], lipid profile, vitamin C [10] and antioxidant enzymes like glutathione peroxidase (GPX) [11] and superoxide dismutase (SOD) [12]. Weight and height of all the participants were noted and Body mass index (BMI) was calculated using the formula = weight (kg) / height^2 (m)

Student's T-Test was used to find out the significance of difference of means.

3. Results

Table 1 shows the anthropometric data viz, age, BMI and BMD.

Table 2 depicts a highly significant decrease (p value <0.001) in the antioxidant enzymes and vitamin C and a highly significant increase (p value <0.001) in the P-MDA in postmenopausal osteoporotic women as compared to the controls.

Table 3 shows a highly significant increase (p value <0.001) in the total cholesterol (TC), triglyceride (TG), and low density lipoprotein cholesterol (LDL- c) and a significant increase (p value <0.01) in very low density lipoprotein cholesterol (VLDL- c). A significant decrease in high density lipoprotein cholesterol (HDL- c) levels in the study group as compared to the control group has also been observed.

Table: 1 Comparison of anthropometric data of pre and postmenopausal osteoporotics

Premenopausal control group (N=56)			Postmenopausal osteoporotics study group (N=56)		p value
	MEAN	SD	MEAN	SD	
Age	36.41	3.98	64	8.78	<0.001
BMI (kg/m2)	24.07	4.5	27.8	6.01	<0.001
BMD (T score)	-0.15	0.91	-2.58	0.73	<0.001

Table: 2 Comparison of antioxidants in pre and postmenopausal osteoporotic women

Premenopausal control group (N=56)			Postmenopausal osteoporotics study group (N=56)		p value
	MEAN	SD	MEAN	SD	
Vitamin C Umol/L	56.50	9.46	35.84	9.8	<0.001
GPX (U/dl Hb)	11.27	0.9	2.56	0.56	<0.001
SOD U/mg	16.67	0.60	4.4	0.54	<0.001
P MDA nmol/ml	2.01	0.27	6.01	0.49	<0.001

Table: 3 Comparison of lipid profile in pre and postmenopausal osteoporotic women

Premenopausal control group (N=56)			Postmenopausal osteoporotics study group (N=56)		p value
	MEAN	SD	MEAN	SD	
TC mg/dl	162.76	12.07	179.84	12.6	<0.001
TG mg/dl	126.39	8.74	137.11	7.28	<0.001
HDL-c mg/dl	44.98	5	38.62	5.4	<0.001
LDL-c mg/dl	68.76	8.6	88.58	10.64	<0.001
VLDL-c mg/dl	15.64	3.42	17.31	3.31	<0.01

4. Discussion and Conclusion

The Present study investigated the status of plasma antioxidants and lipid profile in postmenopausal osteoporotic females. Oxidative stress develops in the postmenopausal osteoporotic women due to deficiency of estrogen. Estrogen is a powerful antioxidant which prevents lipid per oxidation. Dyslipidemia in menopause is a known feature in women. In postmenopausal osteoporotic women lack of estrogen along with aging is responsible for the increased

concentration of TC, TG, VLDL-c and LDL-c and decreased concentration of HDL-c which in turn contributes to the atherogenic lipid profile. This finding is consistent with the findings of Abbey et.al [13], the cardio protective effect of estrogen is attributed to its effect on cholesterol metabolism and deposition contributing to the prevention of atherosclerosis.

Vitamin C, a crucial cofactor in the maturation of collagen whose triple helix stabilization depends on the hydroxylation of proline, a metabolic step requiring vitamin C [14] is the antioxidant with most significant evidence for a possible influence on bone formation or bone loss. It is an essential nutrient for collagen formation and normal bone development. Data from various observational studies, albeit not consistently, seem to carve out a positive role for vitamin C in contrasting age related bone loss in women in their early and mid postmenopausal years, especially if they were calcium repleted but not estrogen repleted [15, 16]. Our study shows a significant reduction in the levels of vitamin C, the antioxidant vitamin in the postmenopausal osteoporotic women. Vanita et.al also reported similar result and further found no significant increase vitamin C levels post antiresorptive therapy in the postmenopausal osteoporotic group [17].

A group of antioxidants present in erythrocytes and plasma prevent lipid per oxidation. The level of GPX and SOD are found to be significantly decreased in the postmenopausal osteoporotic women. Similar results have been obtained by Maggio et.al [18].

We measured plasma MDA as marker of free radical mediated lipid per oxidation and found significant difference between the groups. This finding is in accordance with the results of a recent study reporting increased levels of MDA in a limited sample of postmenopausal osteoporotic women [19].

The low antioxidant levels and high MDA as obtained in the study suggest that antioxidant deficiency has a negative impact on bone mass.

Several potential mechanisms underlie this relationship. It has been proposed that low intracellular and probably interstitial levels of antioxidants are a signal, i.e., a consequence of increased osteoclastogenic activity and bone turnover. Alternatively it is also true that low levels of intracellular antioxidants may amplify osteoclastogenesis through excess free radicals and reactive oxygen intermediates.

It is concluded that postmenopausal osteoporotics have lower antioxidant defenses compared to premenopausal women and oxidative stress in the study group is responsible for the oxidative injury resulting in pathogenesis of osteoporosis. The mechanism underlying antioxidants and its relevance to pathophysiology of osteoporosis deserve further research.

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